

# Efficacy and Safety of EMLA Cream in Reducing Pain During Intrauterine Device Insertion: Systematic Review and Meta-Analysis of Randomized Controlled Trials

Review  
Article

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## ABSTRACT

**Introduction:** Intrauterine devices (IUDs) are a safe and effective method of reversible contraception. However, pain and anxiety during IUD insertion may limit its global utilization. Evidence for EMLA (lidocaine-prilocaine) cream efficacy in pain reduction with IUD insertion is limited.

**Objective:** To systematically and meta-analytically evaluate the efficacy and safety of EMLA (5% lidocaine-prilocaine cream) compared to placebo in reducing pain during intrauterine device (IUD) insertion.

**Methods:** We comprehensively searched PubMed, Scopus, Web of Science, and Cochrane Library till May 2024. We included only randomized placebo-controlled trials (RCTs) and used Cochrane Risk of Bias Tool 2 for quality assessment. Our primary outcome was pain during IUD insertion and uterine sounding, while provider ease of IUD insertion, women's satisfaction, and drug side effects are secondary outcomes. We summarized pooled outcomes as mean difference (MD) or risk ratio (RR) with a 95% confidence interval (CI).

**Results:** Four studies were included (N=432 women) with a low risk of bias overall. EMLA cream significantly lowered pain at tenaculum placement (MD= -1.68, 95% CI [-2.5, -0.86],  $p < 0.0001$ ), uterine sounding (MD= -1.8, 95% CI [-2.51, -1.08],  $p < 0.00001$ ), and IUD insertion (MD= -1.74, 95% CI [-2.63, -0.85],  $p = 0.0001$ ) than placebo. The EMLA cream lowered the need for additional analgesia (RR= 0.2, 95% CI [0.07, 0.57],  $p = 0.002$ ) and increased provider ease of IUD insertion (MD= -1.4, 95% CI [-1.68, -1.13],  $p < 0.00001$ ). Side effects were comparable between both groups.

**Conclusion:** EMLA cream is a safe, effective pain-lowering medication with improved patient satisfaction during IUD insertion. The reduction in pain scores was clinically significant, with a low risk of bias.

**Key Words:** EMLA cream; intrauterine device; lidocaine-prilocaine; pain relief; placebo

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## INTRODUCTION

The global public health issue of unintended pregnancy affects a large proportion of women and their families, causing substantial health, economic, and social problems<sup>[1]</sup>. Effective long-acting contraceptives could significantly reduce the incidence and consequences of unplanned pregnancy. Intrauterine devices (IUDs) are safe, effective, low-cost, long-acting reversible contraceptives (LARC) comparable to tubal sterilization<sup>[2]</sup>. The IUDs do not necessitate continuous patient effort to ensure long-term efficacy with rapid return of fertility upon device removal.

Despite their efficacy, the IUD insertion process might be accompanied by varying levels of discomfort and pain, which may deter some women from choosing this reliable contraceptive method. In a prospective survey, 77% of

nulliparous women reported moderate to severe pain, and 17% may experience severe pain during IUD insertion, necessitating pain management strategies<sup>[3,4]</sup>.

The latest Center for Disease Control (CDC) guidelines suggest that IUD utilization might be hindered by high anticipated pain and healthcare practitioners' concerns about difficult insertion<sup>[5]</sup>. Pain may occur during tenaculum placement, uterine sounding, IUD insertion, and contact with the uterine fundus<sup>[6]</sup> and could be aggravated by nulliparity, age >30, longer time interval since last pregnancy or menstruation, and absence of current breastfeeding<sup>[7]</sup>. By reducing pain with IUD insertion, patients are more satisfied with a broader adoption of IUD, and clinicians can execute the procedure more quickly and with fewer complications.

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Currently, there are no established and universally accepted standards for managing pain with IUD placement. Common pain management techniques often involve non-steroidal anti-inflammatory drugs (NSAIDs), preprocedural misoprostol to soften the cervix, and local anesthetics in the form of intracervical gel, cervical block, and paracervical block(2). Various modalities may be utilized to administer local anesthesia during gynecological procedures, including intrauterine, intracervical, paracervical, and topical applications(2). Different local anesthesia approaches aim to minimize discomfort by numbing the cervix and surrounding tissues.

The EMLA cream combines lidocaine (2.5%) and prilocaine (2.5%), forming a eutectic mixture that has emerged as a promising solution to mitigate pain during IUD insertion<sup>[2-8]</sup>. When applied topically, it provides local anesthesia by inhibiting nerve impulse conduction through sodium channel blockade. When applied to the genital mucous membrane, EMLA exhibits a quick onset of action, typically within 5-10 minutes, and provides pain relief for approximately 15-20 minutes. Therefore, it is advisable to perform gynecological procedures shortly after application to maximize the pain-relieving effectiveness<sup>[9]</sup>.

EMLA is highly tolerable and offers efficient pain relief for superficial surgical and gynecological procedures, such as genital wart removal, vulval biopsies, laser treatment of cervical intraepithelial neoplasia (CIN) lesions, hysterosalpingography, and hysteroscopy<sup>[10-12]</sup>. A limited number of RCTs investigated the analgesic effectiveness of EMLA during IUD insertion<sup>[8,13-15]</sup>. Although those studies<sup>[8,13-15]</sup> found EMLA cream effective in lowering IUD insertion pain, the small sample size for those individual RCTs constrained the robustness and validity of the findings and led to inconsistencies.

Currently, no systematic review and meta-analysis have been carried out to gather evidence and provide strong recommendations on the analgesic effectiveness of EMLA in IUD procedures. Hence, this study aims to conduct a comprehensive review and meta-analysis of all randomized controlled trials (RCTs) that evaluated EMLA's pain-relieving effectiveness and safety during intrauterine device (IUD) insertion.

## **METHODS**

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This systematic review and meta-analysis followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines<sup>[16]</sup>. We registered the study protocol in the Open Science Framework (OSF) registry with a registration DOI: (<https://doi.org/10.17605/OSF.IO/5V3XF>). No ethical approval was needed because this was a systematic review and meta-analysis.

## **Literature Search**

We searched four electronic databases (PubMed, Cochrane Library, Scopus, and Web of Science) from database inception till May 2024, using the following search strategy: (lidocaine OR prilocaine OR EMLA OR (lidocaine-prilocaine cream) OR (Lidocaine Prilocaine) OR Oraqix) AND ((intrauterine device) OR (intrauterine devices) OR IUD OR IUDs). No language, publication date, or country restrictions were made.

## **Study Selection**

We included all publications that satisfied our PICOS criteria in our review: (P) Patients: women who received Cu-IUD or levonorgestrel-releasing intrauterine system (LNG-IUS) for contraception, (I) Intervention: EMLA (lidocaine-prilocaine) cream, (C) Comparator: placebo, (O) Outcomes: efficacy and safety endpoints. Our primary outcomes were pain during uterine sounding and IUD insertion. Our secondary outcomes included pain at tenaculum insertion, after IUD insertion (5- 10 min), ease of IUD insertion, need for additional analgesics, and postprocedural bleeding or spotting. (S) Study design: RCTs. Exclusion criteria included IUD insertion for non-contraceptive indications, any drug other than EMLA, non-randomized trials, conference proceedings, abstracts, articles without full texts, and non-English articles.

We used EndNote software to manage all the retrieved citations and remove duplicates. After obtaining unique records, all citations underwent a two-phase screening process. Title and abstract screening comprised the initial phase, while full-text screening comprised the subsequent phase. In addition, we thoroughly examined the reference lists of all eligible articles to identify any articles that could potentially be relevant. Two reviewers performed the screening phases independently, and disagreements were settled by discussion with an experienced author.

## **Quality Assessment**

Study quality was assessed using the Cochrane Risk of Bias tool 2 (ROB 2)(17). It consists of five main domains: randomization process, deviation from the intended interventions, missing outcome data, measurement of outcome, and the last one is selection of the reported result. Every study will be classified as low risk, some concern, or a high risk of bias. Also, we assessed evidence quality using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) guidelines<sup>[18,19]</sup>.

## **Data Extraction**

Two reviewers independently used a pre-formatted Excel Worksheet to extract the baseline characteristics of

participants, the study characteristics, the study outcomes, and the quality assessment. The baseline and study characteristics included mainly the study ID, study location, type of IUD, study groups, the sample size for each group, EMLA cream dose, participants' ages, Body mass index (BMI), residence, educational level, parity, menstrual pain, breastfeeding, office gynecological procedures, and any history of cesarian deliver (CD), vaginal delivery (VD), miscarriage, or previous IUD insertion.

Data about drug efficacy and safety included pain at tenaculum placement, uterine sounding, IUD insertion, 5-10 minutes postprocedure, ease of IUD insertion, need for additional analgesics, postprocedural bleeding or spotting, and side effects of study medication. Pain scores were evaluated according to the 10-cm Visual Analog Scale (VAS). This scale is graded from 0 to 10, where 0 means no pain at all and 10 is the worst pain imaginable<sup>[13]</sup>. The ease of insertion score (ES) is a VAS-like scale that ranges from 0 to 10, with 10 representing a very difficult insertion and 0 representing a very easy insertion<sup>[13,14]</sup>. Discussion with a senior author settled Any disagreements between authors in data extraction or risk of bias assessment.

### Data Analysis

Meta-analysis was done with Review Manager Software 5.4. We employed the inverse variance approach to analyze continuous data and presented the results as the mean difference (MD) and a 95% confidence interval (CI).

We employed the Mantel-Haenszel technique to analyze dichotomous data, and the results were presented as a risk ratio (RR) along with a 95% confidence interval (CI). Statistical heterogeneity was considered significant when the chi-square *p-value* was  $< 0.1$  and the I-square statistic (I<sup>2</sup>) was  $> 50\%$ (20). Homogeneous data was analyzed using a fixed effect model, while heterogeneous data was analyzed using a random effect model.

Due to the small number of papers included in our review (n=4), we were unable to evaluate publication bias using Egger's test, which requires a minimum of 10 studies<sup>[21]</sup>. The Wan *et al.* technique was employed to derive the mean and standard deviation (SD) from the median and interquartile range<sup>[22]</sup>.

## RESULTS

### Search Results and Study Selection.

The literature search yielded a total of 722 records. After removing duplicates, 526 unique records were evaluated by title and abstract screening. We excluded 518 records from the first screening phase, leaving only 8 articles to be assessed by the full-text screening. Finally, 4 RCTs were eligible to be included in our review<sup>[8,13-15]</sup>. The PRISMA flowchart of screening and study selection is presented in (Figure 1)

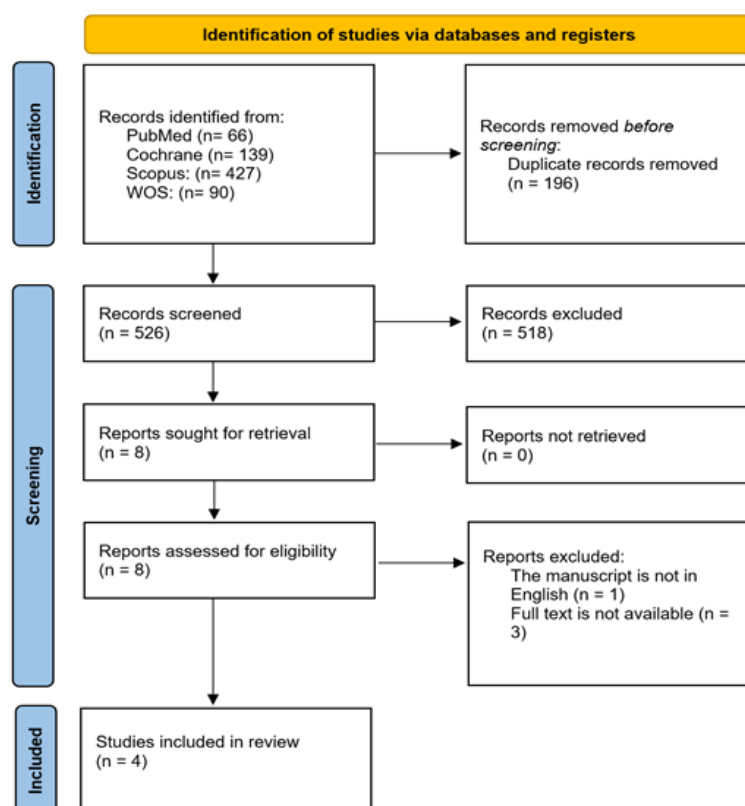


Fig.1 Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) flow diagram and chart.

### Characteristics of Included Studies

We incorporated four RCTs comprising a collective sample size of 432 patients. Two trials were conducted in Egypt<sup>[13,14]</sup>, while the other two were conducted in Iran<sup>[8-15]</sup>. All the trials used copper IUD as a contraceptive method except Hashem *et al.*<sup>[13]</sup>, which used LNG-IUS. Furthermore, three trials included women who had a previous history of either CD or VD<sup>[8,14,15]</sup>. Hashem *et al.* was the only study that included women delivered previously only by cesarean section<sup>[13]</sup>. The duration of EMLA cream application was consistent among the studies; it ranged from 5 to 7 minutes before the

procedure. (Tables 1, 2) display the summary and baseline characteristics of included studies.

### Risk of Bias and Quality of Evidence

All the studies had an overall low risk of bias except Boryri *et al.*<sup>[15]</sup>, which showed some concerns regarding the randomization process. Also, Boryri *et al.*<sup>[15]</sup> did not report data regarding the blinding process. Since our primary outcome is subjective, a lack of blinding could have affected their study results (Figures 2, 3). The GRADE approach in (Table 3) illustrates the quality of evidence.

**Table 1.** Summary of the included studies.

Study ID	Study Design	Center	Intervention	Number in each group	Type of IUD	dose of the cream
Tavakolian <i>et al.</i> 2015	RCT	Hamedan clinic, Iran.	EMLA cream	46	COPPER IUD	5 g
			Placebo	46		NA
Boryri <i>et al.</i> 2017	RCT	Imam Javad Health Center, Zahedan, Iran.	EMLA cream	40	COPPER IUD	5 g
			Placebo	40		NA
Abbas <i>et al.</i> 2016	RCT	Assiut Women's Health Hospital, Assiut, Egypt.	EMLA cream	60	COPPER IUD	4 ML
			Placebo	60		NA
Hashem <i>et al.</i> 2022	RCT	Seha Hospital (Algezeerah), Giza, Egypt.	EMLA cream	70	LNG-IUD	5 ML
			Placebo	70		NA

RCT; Randomized controlled trial, IUD; Intra uterine device, NA; Not available, LNG; Levonorgestrel.

**Table 2.** Baseline characteristics of the included studies.

ID	Intervention	N	Age, M ±SD	BMI (kg/ m <sup>2</sup> ), M ±SD	Residence, c			Education, N (%)						Parity, M ±SD	Previous CD, N (%)	Previous VD, N (%)	Previous miscarriages, N (%)	History of IUD insertion, N (%)	Breastfeeding, N (%)	Menstrual pain	Office gynecological procedures
					Urban	Rural	Illiterate	Preparatory or Secondary school	University												
Tavakolian <i>et al.</i> 2015	EMLA cream	46	26.78 ±4.07	NA	NA	NA	NA	NA	NA	NA	22 (47.8)	24 (52.2)	NA	15 (32.6)	29 (63)	NA	2 (4.3)				
	Placebo	46	26.43 ±4.52	NA	NA	NA	NA	NA	NA	NA	22 (47.8)	24 (52.2)	NA	15 (32.6)	29 (63)	NA	0(0)				
Boryri <i>et al.</i> 2017	EMLA cream	40	26.75 ±6.33	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	
	Placebo	40		NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Abbas <i>et al.</i> 2016	EMLA cream	60	31.1 ±6.2	NA	23 (38.3)	37 (61.7)	0	28 (46.7)	20 (33.3)	38 (63.3)	32 (53.3)	19 (31.7)	34 (56.7)	NA	11 (18.3)	9 (15.0)					
	Placebo	60	31.4 ±6.7	NA	27 (45.0)	33 (55.0)	0	40 (66.7)	14 (23.3)	39 (65.0)	27 (45.0)	18 (30.0)	27 (45.0)	NA	9 (15.0)	8 (13.3)					
Hashem <i>et al.</i> 2022	EMLA cream	70	28.5 ±6.1 ±4.0	23.9 ±4.0	40 (57.1)	30 (42.9)	4 (5.7)	22 (31.5)	17 (24.3)	70 (100)	0	14 (20.0)	27 (38.6)	60 (85.7)	31 (44.3)	NA					
	Placebo	70	28.5 ±5.3 ±2.9	24.1 ±2.9	45 (64.3)	25 (35.7)	4 (5.7)	19 (27.1)	25 (35.7)	70 (100)	0	20 (28.6)	24 (34.3)	56 (80.0)	42 (59.9)	NA					

**M** ±SD; Mean ±standard deviation, **N**; Number, **N (%)**; Number (percentage), **CD**; Cesarean delivery, **VD**; Vaginal delivery, **NA**; Not available.

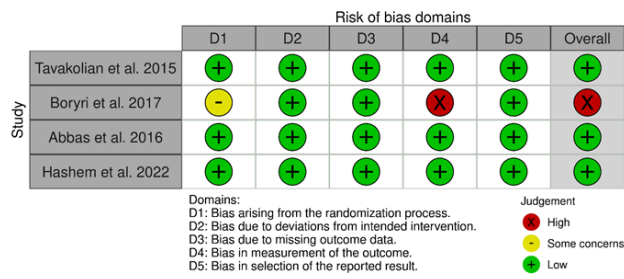


Fig 2. Risk of bias summary of included studies.

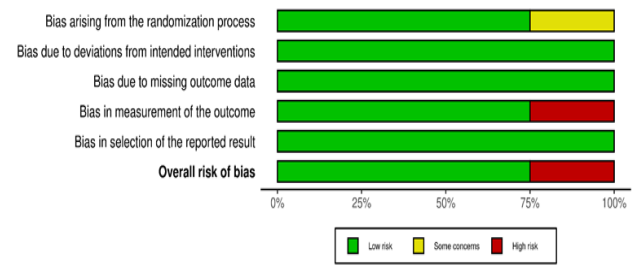


Fig 3. Risk of bias graph of included studies.

Table 3: The quality of evidence assessed by the GRADE approach

No of studies	Study design	Risk of bias	Certainty assessment				Other considerations	No of patients		SMD or RR, 95% CI	Certainty
			Inconsistency	Indirectness	Imprecision	EMLA cream		Placebo cream			
4	RCT	Serious <sup>a</sup>	Not Serious <sup>b</sup>	Not serious	Serious <sup>c</sup>	None	216	216	SMD= -1.68 (-2.5, -0.86)	⊕⊕Low	
Pain at tenaculum insertion											
4	RCT	Serious <sup>a</sup>	Not Serious <sup>b</sup>	Not serious	Serious <sup>c</sup>	None	216	216	SMD= -1.8 (-2.51, -1.08)	⊕⊕Low	
Pain at uterine sounding											
4	RCT	Serious <sup>a</sup>	Not Serious <sup>b</sup>	Not serious	Serious <sup>c</sup>	None	216	216	SMD= -1.74 (-2.63, -0.85)	⊕⊕Low	
Pain at IUD insertion											
2	RCT	Not serious	Not serious <sup>b</sup>	Not serious	Serious <sup>d</sup>	None	130	130	SMD= -0.76 (-1.01, -0.51)	⊕⊕⊕Moderate	
Pain after IUD insertion (5- 10 min)											
2	RCT	Not serious	Not serious	Not serious	Serious <sup>d</sup>	None	130	130	SMD= -1.4 (-1.68, -1.13)	⊕⊕⊕Moderate	
Ease of IUD insertion											
2	RCT	Not serious	Not serious	Not serious	Serious <sup>e</sup>	None	130	130	RR= 0.20 (0.07, 0.57)	⊕⊕⊕Moderate	
Need for additional analgesics											
2	RCT	Not serious	Not serious	Not serious	Serious <sup>e</sup>	None	130	130	RR= 0.57 (0.25, 1.3)	⊕⊕⊕Moderate	
Postprocedural bleeding or spotting											

RCT; Randomized controlled trial, SMD; Standardized mean difference, RR; Risk ratio, CI; Confidence interval.

a One study had a high risk of bias and could affect the results.

b There was heterogeneity that could be explained or solved by sensitivity analysis.

c Wide confidence interval.

d The analysis included small number of patients.

e The analysis included a small number of patients with wide confidence interval.

### Efficacy Outcome: Pain at Tenaculum Insertion

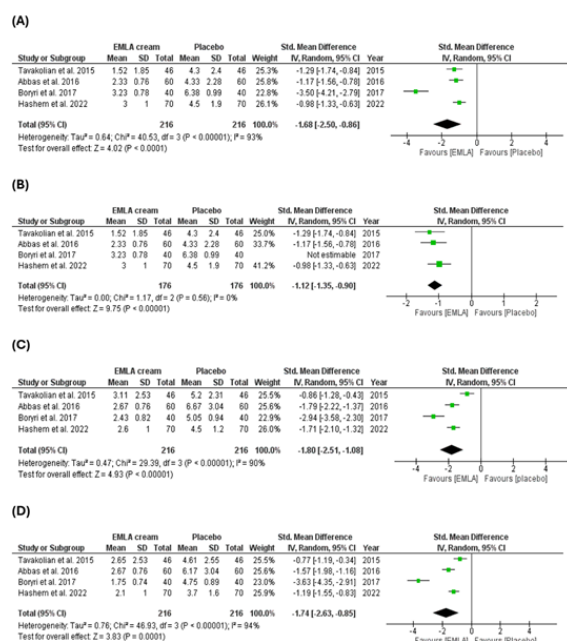
Four studies reported pain at tenaculum insertion<sup>[8,13-15]</sup>, involving 432 patients divided equally between the EMLA and placebo groups. The EMLA group exhibited significantly reduced pain scores compared to the placebo group (MD= -1.68, 95% CI [-2.5, -0.86],  $p < 0.0001$ ; Low-quality evidence). Pooled data showed significant heterogeneity ( $p < 0.00001$ ,  $I^2 = 93%$ ) (Figure 4A). This heterogeneity was resolved by excluding Boryri *et al.*<sup>[15]</sup> ( $p = 0.56$ ,  $I^2 = 0%$ ) (Figure 4B).

### Efficacy Outcome: Pain at Uterine Sounding

Pain at uterine sounding was reported in four studies<sup>[8,13-15]</sup> (N=216 EMLA group and N=216 placebo group). The EMLA group had significantly lower pain VAS levels compared to the placebo group (MD= -1.8, 95% CI [-2.51, -1.08],  $p < 0.00001$ ; Low-quality evidence). The pooled data showed heterogeneity ( $p < 0.00001$ ,  $I^2 = 90%$ ) (Figure 4C).

### Efficacy Outcome: Pain at IUD Insertion

Meta-analysis of four studies<sup>[8,13-15]</sup> (N= 216 EMLA group and 216 placebo group) showed significantly reduced pain levels in EMLA group more than placebo group (MD= -1.74, 95% CI [-2.63, -0.85],  $p = 0.0001$ ; Low-quality evidence). The pooled studies showed significant heterogeneity ( $p < 0.00001$ ,  $I^2 = 94%$ ) (Figure 4D).



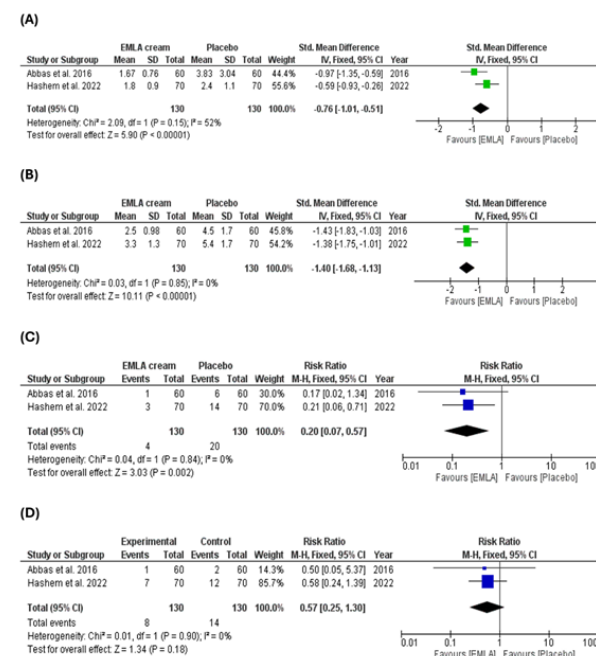
**Fig. 4.** Forest plots showing the standardized mean difference (SMD) for pain at tenaculum insertion [A], pain at tenaculum insertion after excluding Boryri *et al.* [B], pain at uterine sounding [C], and pain at intrauterine device (IUD) insertion [D] between EMLA and placebo groups.

### Efficacy Outcome: Pain after IUD Insertion (5- 10 min)

Postprocedural pain level was reported in two studies<sup>[13,14]</sup> with 130 patients in EMLA group and 130 patients in placebo group. The pooled analysis showed a significant reduction in pain level in the EMLA group than in the placebo group (MD= -0.76, 95% CI [-1.01, -0.51],  $p = 0.0001$ ; Moderate-quality evidence). The pooled results showed a moderate heterogeneity ( $p = 0.15$ ,  $I^2 = 52%$ ) (Figure 5A).

### Efficacy Outcome: Ease of IUD Insertion

The healthcare providers reported ease of IUD insertion in two studies<sup>[13,14]</sup> with 130 women in EMLA group and 130 women in placebo group. In the meta-analysis, the EMLA group had easier IUD insertion than the placebo group (MD= -1.4, 95% CI [-1.68, -1.13],  $p < 0.00001$ ; Moderate-quality evidence). Pooled results were homogenous ( $p = 0$ ,  $I^2 = 85%$ ) (Figure 5B).



**Fig. 5.** Forest plots showing the standardized mean difference (SMD) for Pain after IUD insertion (5- 10 min) [A], ease of IUD insertion [B], need for additional analgesics [C], and postprocedural bleeding or spotting [D] between EMLA and placebo groups.

### Efficacy Outcome: Need for Additional Analgesics

This outcome was reported in two studies<sup>[13,14]</sup> with 130 participants in EMLA group and 130 participants in placebo group. The EMLA group had a substantially lower number of women requiring additional analgesia, as indicated by the pooled analysis (RR= 0.2, 95% CI [0.07, 0.57],  $p = 0.002$ ; Moderate-quality evidence). The pooled results were homogenous ( $p = 0$ ,  $I^2 = 84%$ ).

### Safety Outcomes: Postprocedural Bleeding or Spotting

Two studies<sup>[13,14]</sup> reported postprocedural bleeding or spotting. A non-significant difference was seen between the two study groups, according to the pooled analysis (RR= 0.57, 95% CI [0.25, 1.3],  $p = 0.18$ ; Moderate-quality evidence). However, the results were homogenous ( $p = 0.9$ ,  $I^2 = 0\%$ ).

### Safety Outcomes: Side Effects of Study Medication

Only two trials reported drug side effects<sup>[13,14]</sup>, with 130 EMLA and 130 placebo patients. Hashem *et al.*<sup>[13]</sup> reported side effects such as abdominal cramps, nausea, vomiting, fever, shivering, headache, diarrhea, and a burning sensation in 11 patients of EMLA group and 15 patients in placebo group. While Abbas *et al.*<sup>[14]</sup> reported no side effects in both groups.

## DISCUSSION

Four RCTs assessing EMLA cream's ability to reduce pain during IUD insertion were included in our study. Our meta-analysis showed that women who used EMLA cream had significantly lower pain scores during and after IUD placement than those who had a placebo. The reduction in pain was achieved during tenaculum placement, the sounding of the uterus, and during IUD insertion. In the EMLA group, IUD insertion was easier, women were more satisfied, and they needed less analgesia. Side effects were few and comparable in EMLA group and placebo group. Our included studies were of high quality with a low risk of bias, and most outcomes were homogenous.

Todd *et al.*<sup>[23]</sup> found that a 13-mm VAS difference (95% CI 10 to 17 mm) was the least clinically significant change in acute pain intensity. In other trials, The minimum clinically significant difference (MCSD) for pain reduction was a 15 mm mean difference in the 100-mm VAS<sup>(24,25)</sup>. So, our study found clinically significant pain reduction with EMLA cream during IUD insertion (MD=1.74).

IUD insertion can be challenging and may be linked to extreme anxiety and pain, and Approximately 50% of individuals experience moderate to severe discomfort while undergoing IUD insertion<sup>[26]</sup>. Given its contraceptive efficacy and acceptability, various trials have investigated different pharmacological and non-pharmacological techniques for reducing IUD insertion pain. However, the results were mixed and non-conclusive. While some pharmacological drugs appeared as effective pain-lowering options, such as Lidocaine-prilocaine cream, dinoprostone, and 600 µg of vaginal misoprostol, others failed to lower pain with IUD insertion, such as 2% topical lidocaine gels, 400 µg of misoprostol, or ibuprofen<sup>[27,28]</sup>.

Local anesthetics efficacy in lowering IUD insertion pain was controversial. Paracervical lidocaine injection lowers IUD insertion pain<sup>[29]</sup> but not tenaculum application pain. The lidocaine needle injection is also painful, making this option not the best for pain reduction with IUD insertion<sup>[30]</sup>. Lidocaine spray effectively alleviates pain associated with tenaculum and IUD placement<sup>[31]</sup>. Applying spray is a quick, non-invasive, and easy process<sup>[30,32]</sup>. Studies found that cervical lidocaine gel does not have any significant impact in reducing the overall pain scores during intrauterine device (IUD) insertion<sup>[26,33,34]</sup>. Perez-Lopez *et al.*<sup>[35]</sup> systematic review and meta-analysis (11 RCTs; 1458 women ) evaluated the impact of uterine mucosal or paracervical lidocaine on IUD insertion pain. Lidocaine resulted in decreased visual pain scale (VPS) scores throughout tenaculum placement (MD -0.99), IUD insertion (MD -1.26), and immediately following IUD insertion (MD -1.25).

EMLA Cream consists of amide-type local anesthetic drugs, lidocaine, and prilocaine. It provides relatively rapid and effective analgesia when applied to the female genital mucosa during various clinical procedures in that area<sup>[9]</sup>. EMLA cream's role in pain relief during IUD insertion was studied in previous RCTs. Hashem *et al.*<sup>[13]</sup> reported that lidocaine-prilocaine (LP) cream resulted in a clinically significant reduction in pain during IUD insertion and 10 min postprocedure. Abbas *et al.*<sup>[14]</sup> and Tavakolian *et al.*<sup>[8]</sup> found EMLA cream an effective and safe option for managing pain with IUD insertion. Additionally, Compared to ibuprofen and placebo, EMLA cream reduces pain safely at all stages of IUD insertion<sup>[15]</sup>.

This analgesic effect was confirmed in a recent network meta-analysis by Samy *et al.*<sup>[2]</sup> study, in which they found that topically applied lidocaine-prilocaine cream is the most effective and highest-ranked medication, particularly at tenaculum placement and during IUD insertion. However, this evidence was derived from meta-analyzing two studies only. Considering the beneficial use of EMLA for topical application, the adverse effects of EMLA are generally safe<sup>[9]</sup>.

The EMLA cream proved successful in lowering pain during different gynecological and obstetric procedures. In Abu-Zaid *et al.*<sup>[12]</sup> meta-analysis, EMLA cream significantly lowered pain perception during cervical tenaculum and cannula instrumentation during hysterosalpingography (HSG)(MD = -1.53) and 24 h after HSG completion (MD = -1.30) with no observed local or systemic adverse effects. Similarly, Abbas *et al.*<sup>[36]</sup> reported that both EMLA cream and local perineal infiltration anesthesia had comparable results regarding pain reduction scores during perineal repair following vaginal birth; however, the perineal repair time was shorter, and patient satisfaction was higher with EMLA cream.



Topical EMLA cream application was also an effective analgesic option for reducing pain during vulvar biopsy with improved patient satisfaction<sup>[3]</sup> and during speculum application in postmenopausal women, where EMLA group had lower pain and distress scores than the lubricating gel and control groups<sup>[38]</sup>. Conversely, Grosse-Steffen *et al.*<sup>[39]</sup> found that EMLA cream did not decrease postoperative pain after cesarean delivery or time to mobilization or discharge. Additionally, in Arnau *et al.*<sup>[40]</sup> RCT, topical EMLA does not reduce diagnostic or operative hysteroscopy pain. However, the EMLA group had significantly fewer procedure discontinuation rates. These contradictory findings could be due to a low concentration of the anesthetic substance and the short duration of local anesthetic application.

### Study Strengths and limitations

Our review had several strengths. This meta-analysis is the first to assess the effectiveness of EMLA in relieving discomfort during IUD insertion. Our study effectively addresses the issue of limited sample sizes in earlier studies, allowing for more reliable findings to be drawn. We selected only RCTs to ensure high-quality data reporting. Most of our outcomes were homogenous, and most of the studies included were of high quality and had a low risk of bias.

However, our study was limited by the small number of included RCTs and their sample sizes, and some reported outcomes had significant heterogeneity. Another limitation is the subjectivity in reporting outcomes, such as difficulty with IUD insertion and pain perception. However, no objective parameters are available. There is a lack of sufficient data reporting on the side effects of the study drug. Larger RCTs are needed to assess EMLA's short-term and long-term analgesic efficacy and safety and compare them to placebo and active comparators.

### CONCLUSION

The EMLA cream is a safe, effective pain-lowering medication during IUD insertion. The reduction in pain scores was clinically significant, with a low risk of bias.

### CONFLICT OF INTERESTS

There are no conflicts of interest

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